1632

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Washington, D.C. 20231

On February 4, 2003

DELTAGEN, INC.

By: Deborah A. Mojarro

PATENT
Attorney Docket No.: R-881

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

KEITH D. ALLEN

Application No.: 10/005,216

Filed: December 4, 2001

For: TRANSGENIC MICE CONTAINING TRP6 CALCIUM ION CHANNEL GENE DISRUPTIONS

Examiner: Unassigned

Art Unit: 1632

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT UNDER 37 CFR §1.97 and §1.98

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

The references cited on attached form PTO/SB/08B are being called to the attention of the Examiner. Copies of the references are enclosed. It is respectfully requested that the cited references be expressly considered during the prosecution of this application, and the references be made of record therein and appear among the "references cited" on any patent to issue therefrom.

Each item of information contained in the information disclosure statement was cited in a communication mailed from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of this information disclosure statement.

As provided for by 37 CFR 1.97(g) and (h), no inference should be made that the information and references cited are prior art merely because they are in this statement and no representation is being made that a search has been conducted or that this statement encompasses all the possible relevant information.

Applicant believes that no fee is required for submission of this statement, since it is being submitted prior to the first Office Action. However, if a fee is required, the Commissioner is authorized to deduct such fee from the undersigned's Deposit Account No. 50-1271. Please deduct any additional fees from, or credit any overpayment to, the above-noted Deposit Account.

Respectfully submitted,

Robert J. Driscoll, Reg. No. 47,536

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RJD/dam

PTO/SB/08B (10-01)
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Substitute for form 1449B/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet 1 of 1

Complete if Known	
Applicati n Number	10/005,216
Filing Date	December 4, 2001
First Named Inventor	Keith D. Allen
Art Unit	1632
Examiner Name	Unassigned
Attorney Docket Number	R-881

OTHER PRIOR ART -- NON PATENT LITERATURE DOCUMENTS

Examiner Initials *	Cite No.[1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T[2]
	3	X. WU et al., "FUNCTIONAL SIGNIFICANCE OF HUMAN trpl AND trp3 IN STORE-OPERATED Ca $^{2+}$ ENTRY IN HEK-293 CELLS" Am. J. Physiol. Cell Physiol., Vol. 278, January 3, 2002, pp. C526-C536	
	4	M. CAPECCHI, "TARGETED GENE REPLACEMENT" Scientific American, Vol. 8, March 1994, pp. 52-59	
	5	S. MANSOUR et al., "DISRUPTIONS OF THE PROTO-ONCOGENE *int-2* IN MOUSE EMBRYO-DERIVED STEM CELLS: A GENERAL STRATEGY FOR TARGETING MUTATIONS TO NON-SELECTABLE GENES" Nature, Vol. 336, November 1988, pp. 348-352	

Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] Applicant's unique citation designation number (optional). [2] Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

PCT

INVITATION TO PAY ADDITIONAL FEES

(PCT Article 17(3)(a) and Rule 40.1)

REGISTERED

To:
DELTAGEN, INC
Attn. Burke, John E.
740 Bay Road
Redwood City, California 94063
UNITED STATES OF AMERICA

Date of mailing (day/month/year): 05/11/2002

Applicant's or agent's file reference: 881 PCT

PAYMENT DUE within 45 ~~months~~/days from the above date of mailing

International application No.: PCT/US 01/ 46656

International filing date (day/month/year): 05/12/2001

Applicant: DELTAGEN, INC.

1. This International Searching Authority

(i) considers that there are 2 *(number of)* inventions claimed in the international application covered by the claims indicated ~~below~~/on the extra sheet:

and it considers that the international application does not comply with the requirements of unity of invention (Rules 13.1, 13.2 and 13.3) for the reasons indicated ~~below~~/on the extra sheet:

(ii) [X] has carried out a partial international search (see Annex) [ ] will establish the international search report on those parts of the international application which relate to the invention first mentioned in claims Nos.:
1-20, 22

(iii) will establish the international search report on the other parts of the international application only if, and to the extent to which, additional fees are paid

2. The applicant is hereby **invited,** within the time limit indicated above, to pay the amount indicated below:

EUR 945,00 (Fee per additional invention) x 1 (number of additional inventions) = EUR 945,00 (total amount of additional fees)

Or, _____ x _____ = _____

The applicant is informed that, according to Rule 40.2(c), **the payment of any additional fee may be made under protest,** i.e., a reasoned statement to the effect that the international application complies with the requirement of unity of invention or that the amount of the required additional fee is excessive.

3. [X] Claim(s) Nos. See annex have been found to be unsearchable under Article 17(2)(b) because of defects under Article 17(2)(a) and therefore have not been included with any invention.

Name and mailing address of the International Searching Authority:
European Patent Office, P.B. 5818 Patentlaan 2
NL-2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer: Joannes Vergoosen

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 206

Continuation of Box 3.

Claims Nos.: 13 20 21 22

Present claims 13 and 20 relate to a compound defined by reference to a desirable characteristic , namely an agent identified by a previously claimed method.
The claims cover all compounds having this characteristic or property, whereas the application provides no support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT (page 27 lines 7-10). In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the product/compound/method/apparatus by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search ha no bases to be carried out for those parts of the claims which appear to be unclear, unsupported and not disclosed,:

Present claim 22 relate to an extremely large number of possibl e compounds/products/methods. In fact, the claims contain so many options, variables, possible permutations and provisos
that a lack of clarity within the meaning of Article 6 PCT arises to such an extent as to render a meaningful search of the claims impossible. Consequently, the search has not been carried out for this part of the application which does not appear to be clear .

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INVITATION TO PAY ADDITIONAL FEES

International application No.
PCT/US 01/46656

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-20 22

A targeting construct comprising (a) a first nucleotide sequence homologous to at least a first portion of an TRP6 gene, (b) a second polynucleotide sequence homologous to at least a second portion of the TRP6 gene and a selectable marker; a method of producing such a targeting construct; a cell comprising a disruption in a TRP6 gene; a non-human transgenic animal comprising a disruption in a TRP6 gene; a cell derived from said animal; a method for producing said transgenic animal; a method for identifying an agent that modulates the expression or fonction of a TRP6 gene using said animal or cell; a method for identifying an agent that ameliorates a phenotype associated with a disruption in a TRP6 gene by administering an agent to a transgenic mouse comprising a disruption in a TRP6 gene, and determining whether the agent ameliorates the above mentioned phenotypes; an agent identified by said methods; phenotypic data associated with a transgenic mouse comprising a disruption in a TRP6 gene, where the phenotypic data is in an electronic database.

2. Claim : 21

An agonist or antagonist of TRP6.

The underlying application to transgenic mice containing targeted TRP6 calcium ion channel gene disruptions, methods for producing them and uses thereof for identifying therapeutical agents.
The document JOURNAL OF BIOLOGICAL CHEMISTRY, volume 272,issue pages published in and cited by the applicant already described the murine TRP6 gene.

In view of this prior art, the problems to be solved by the present application could be defined as follows :

- A first problem may be defined as providing means to study the physiopathology of TRP6 gene.
The described solution provides targeted disruptions in TRP6 gene both in vitro and in transgenic animals.

- A second problem can be defined as providing therapeutical agents to treat TRP6 related pathologies.
. The solution is providing agonists and antagonists of TRP6.

Considering that, in the prior art, TRP6 gene has already been disclosed, and due to the fact that no other technical features can be a priori distinguished which, in the light of the prior art, could be regarded as a special technical feature, the ISA is of the opinion that there is no single inventive concept underlying the plurality of

claimed inventions of the present application in the sense of rule 13.1 PCT. Consequently there is lack of unity and the different inventions, not belonging to a common inventive concept, are formulated as the different subjects on the communication pursuant to Art. 17(3)(a) PCT.

. Annex to Form PCT/ISA/206
COMMUNICATION RELATING TO THE RESULTS OF THE PARTIAL INTERNATIONAL SEARCH

International Application No
PCT/US 01/46656

1. The present communication is an Annex to the invitation to pay additional fees (Form PCT/ISA/206). It shows the results of the international search established on the parts of the international application which relate to the invention first mentioned in claims Nos.:
1-20,22
2. This communication is not the international search report which will be established according to Article 18 and Rule 43.

3. If the applicant does not pay any additional search fees, the information appearing in this communication will be considered as the result of the international search and will be included as such in the international search report.

4. If the applicant pays additional fees, the international search report will contain both the information appearing in this communication and the results of the international search on other parts of the international application for which such fees will have been paid.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WU, X. ET AL.: "Functional significance of human trp1 and trp3 in store-operated Ca2+ entry in HEK-293 cells" AMERICAN JOURNAL OF PHYSIOLOGY AND CELLULAR PHYSIOLOGY, vol. 278, no. 3, 1 March 2000 (2000-03-01), pages c526-c536, XP002220259 the whole document	1-22
Y	CAPECCHI M R: "TARGETED GENE REPLACEMENT" SCIENTIFIC AMERICAN, SCIENTIFIC AMERICAN INC. NEW YORK, US, March 1994 (1994-03), pages 52-59, XP002940139 ISSN: 0036-8733 the whole document	1-22
Y	MANSOUR S L ET AL: "DISRUPTION OF THE PROTO-ONCOGENE INT-2 IN MOUSE EMBRYO-DERIVED STEM CELLS: A GENERAL STRATEGY FOR TARGETING MUTATIONS TO NON-SELECTABLE GENES" NATURE, MACMILLAN JOURNALS LTD. LONDON, GB, vol. 336, 24 November 1988 (1988-11-24), pages 348-352, XP002052220 ISSN: 0028-0836 the whole document	1-5

-/--

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

Annex to Form PCT/ISA/206
COMMUNICATION RELATING TO THE RESULTS OF THE PARTIAL INTERNATIONAL SEARCH

International Application No
PCT/US 01/46656

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
Y	BOULAY GUYLAIN ET AL: "Cloning and expression of a novel mammalian homolog of Drosophila Transient Receptor Potential (Trp) involved in calcium entry secondary to activation of receptors coupled by the Gq class of G protein" JOURNAL OF BIOLOGICAL CHEMISTRY, AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, BALTIMORE, MD, US, vol. 272, no. 47, 21 November 1997 (1997-11-21), pages 29672-29680, XP002213458 ISSN: 0021-9258 cited in the application the whole document	1-22
P,A	INOUE R, OKADA T, ONOUE H, HARA Y, SHIMIZU S, NAITOH S, ITO Y, MORI Y.: "The transient receptor potential protein homologue TRP6 is the essential component of vascular alpha(1)-adrenoceptor-activated Ca(2+)-permeable cation channel." CIRC RES 2001 FEB 16;88(3):325-32, XP002220260 the whole document	1
P,A	WO 01 30798 A (ALLEN KEITH D ;DELTAGEN INC (US); KLEIN ROBERT (US); MOORE MARK (U) 3 May 2001 (2001-05-03) the whole document	1

Patent Family Annex

Information on patent family members

International Application No
PCT/US 01/46656

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 0130798 A	03-05-2001	AU 1343501 A	08-05-2001
		EP 1224199 A1	24-07-2002
		WO 0130798 A1	03-05-2001